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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,843	04/15/2004	Robert T. Lyons	17684 (AP)	2070

51957 7590 12/04/2008

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EXAMINER	
FAY, ZOHREH A	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
12/04/2008	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ROBERT T. LYONS, CHIN-MING CHANG, JOAN-EN CHANG-LIN, JAMES CHANGE and OREST OLEJNIK[1]

Appeal 2008-5416
Application 10/826,843
Technology Center 1600

Decided: December 4, 2008

Before JAMES T. MOORE, *Vice Chief Administrative Patent Judge*, and RICHARD E. SCHAFER and RICHARD TORCZON, *Administrative Patent Judges*.

Opinion for the Board filed by *Vice Chief Administrative Patent Judge*, MOORE, joined by *Administrative Patent Judge,* SCHAFER.

Opinion Concurring, filed by *Administrative Patent Judge,* TORCZON.

MOORE, *Vice Chief Administrative Patent Judge.*

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[1] The real party in interest is Allergan, Inc. (App. Br. 1).

DECISION ON APPEAL

STATEMENT OF CASE

The Appellants appeal under 35 U.S.C. § 134 (2002) from a final rejection of claims 1-19, 21-23 and 26.[2] We have jurisdiction under 35 U.S.C. § 6 (b) (2002).

The Appellants' claims are directed to medicating the interior of the eye using a medicament and a cyclodextrin as a carrier.

Claims 1 and 19 are the only independent claims in the application. The Appellants do not argue any claims separately regarding the enablement or anticipation rejections. Therefore, we select independent claim 1, the method claim, to decide the appeal regarding these rejections. See 37 C.F.R. § 41.37(c)(1)(vii) (2006).

For the obviousness rejection, the Appellants argue claims 16-18 together. Claim 16 is representative, and the remaining claims stand or fall with claim 16.

Claim 1 reads as follows:

> 1. A method comprising topically administering a composition to an eye of a mammal in need thereof, said method being effective in delivering a therapeutically effective amount of a therapeutically active agent to a structure or combination of structures of the eye selected from the vitreous humor and structures posterior to the vitreous humor; said composition comprising;
>
> a. an effective amount of the therapeutically active agent, or a pharmaceutically acceptable salt or prodrug thereof, to provide a therapeutically effective amount

[2] Claims 20, 24, 25, and 27 have been canceled. (App. Br. 2).

of the therapeutically active agent to said structure or combination of structures of the eye, and

b. an effective amount of a cyclodextrin derivative to provide said therapeutically effective amount of said therapeutically active agent to said structure or combination of structures of the eye[,]

wherein the cylodextrin derivative is selected from the group consisting of hydroxypropyl-β-cyclodextrin, hydroxypropyl-γ-cyclodextrin, sulfobutylether-β-cyclodextrin and sulfobutylether-γ-cyclodextrin, hydroxyethyl-β-cyclodextrin, hydroxyethyl-γ-cyclodextrin, dihydroxypropyl-β-cyclodextrin, glucosyl-β-cyclodextrin, diglucosyl-β-cyclodextrin, maltosyl-β-cyclodextrin, maltosyl-γ-cyclodextrin, maltotriosyl-β-cyclodextrin, maltotriosyl-γ-cyclodextrin, dimaltosyl-β-cyclodextrin, and combinations thereof.

(App. Br. 10, Claims Appendix).

Claim 5, from which claim 16 depends, reads as follows:

5. The method of claim 1 wherein said therapeutically active agent is not administered to reduce intraocular pressure.

Claim 16 reads as follows:

16. The method of claim 5 which further comprises hydroxypropylmethylcellulose having a concentration of less than 1%.

(App. Br. 11, Claims Appendix).

THE EVIDENCE

The Examiner relies upon the following as evidence in support of the rejections:

Loftsson	US 5,472,954	Dec. 05, 1995
Guy	US 5,576,311	Nov. 19, 1996

Lyons	WO 02/089815 A2	Nov. 14, 2002

THE REJECTIONS

The following rejections are before us for review:

1. Claims 1-19, 21-23 and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

2. Claims 1-15, 19, 21-23 and 26 stand rejected as being anticipated under 35 U.S.C. § 102(b) over Guy.

3. Claims 1-19, 21-23 and 26 stand rejected as being anticipated under 35 U.S.C. § 102(b) over Lyons.

4. Claims 16-18 stand rejected as being obvious under 35 U.S.C. § 103(a) over the combination of Guy and Loftsson.

We REVERSE the enablement rejection of claims 1-19, 21-23 and 26; AFFIRM the anticipation rejections of claims 1-19, 21-23 and 26; and AFFIRM the obviousness rejection of claims 16-18.

ISSUES

Have the Appellants established that the Examiner erred in determining that the specification does not provide sufficient guidelines to enable of one of ordinary skill in the art to know, without undue experimentation, which therapeutically active agents may be administered by the claimed method?

Have the Appellants established that the Examiner erred in determining that the prior art anticipated a method of topically administering a known topical ophthalmic composition to structures of the eye in or posterior to the vitreous humor?

Have the Appellants established that the Examiner erred in determining that it would have been obvious to one of ordinary skill in the art at the time the invention was made to topically administer a known topical ophthalmic composition to structures of the eye in or posterior to the vitreous humor?

FINDINGS OF FACT

The record supports the following findings of fact by a preponderance of the evidence.

1. The specification describes that "the use of cyclodextrins in pharmaceutical compositions is well known in the art." (Specification p. 3, ll. 7-8).

2. The specification also describes that "[t]he use of cyclodextrin and cyclodextrin derivatives in ophthalmic formulations is also known." (Id. p. 3. ll. 20-21).

3. Additionally, the specification provides numerous examples of "therapeutically active agent[s]," as claimed. (Id. pp. 6-7).

4. Guy describes topical ophthalmic compositions for the treatment of inflammatory conditions of the eye. (Guy 1:8-11).

5. Guy describes that its ophthalmic compositions comprise a therapeutic concentration of a water insoluble or poorly soluble drug and an effective amount of cyclodextrin. (Id. 3:45-67).

6. Guy describes that the therapeutically active drug component may be a nonsteroidal anti-inflammatory drug, an antimicotic, an antiepileptic, an antihistamine, or a locally active steroid, such as prednisolone. (Id. 3:54-66).

7. Guy describes that the cyclodextrin component can be methyl cyclodextrin, glucosyl cyclodextrin, maltosyl cyclodextrin, multiple derivative forms of these cyclodextrins, hydroxypropyl cyclodextrin, beta-hydroxypropyl cyclodextrin, beta cyclodextrin or hydroxyethyl cyclodextrin. (Id. 4:1-4; 5:6-9; Table 2).

8. Lyons describes methods and ophthalmic compositions for the topical delivery of lipophilic drugs to the eye. (Lyons pp. 9-11).

9. Lyons describes that its ophthalmic compositions comprise a therapeutically effective amount of an active drug, such as antibiotics, steroids, e.g., prednisolone, and nonsteroidal anti-inflammatory drugs. (Id. 10-11).

10. Lyons describes that its ophthalmic compositions also comprise cyclodextrins selected from naturally occurring cyclodextrins or their synthetic derivatives that are, "without limitation, formed by alkylation (e.g. methyl- and ethyl-β-cyclodextrin) or hydroxyalkylation of the hydroxyl groups (e.g. hydroxyproply- and hydroxyethyl –derivatives of α-, β-, and γ-cyclodextrin) or by substituting the primary hydroxy groups with saccharides (e.g. glucosyl- and maltosyl-β-cyclodextrin)." (Id. 12).

11. Lyons also describes that its ophthalmic composition comprises a water soluble polymer such as hydroxypropylmethylcellulose (HPMC) (Id. 10).

12. Loftsson describes a method of enhancing the solubilizing and stabilizing effects of cyclodextrin derivatives in cyclodextrin-drug complexes by adding certain polymers. (Loftsson 1:12-15).

13. Loftsson describes that suitable polymers for its method, such as HPMC, are water soluble and acceptable for use in pharmaceuticals. (Id. 7:7-30).

14. Additionally, Loftsson describes that the polymer comprises 0.001-5%, preferably from about 0.01 to about 0.5% of the composition. (Id. 4:21-30).

15. Loftsson also describes that suitable pharmaceuticals for its method include ophthalmic compositions (eye drops) containing agents including anti-glaucoma agent, anti-inflammatory steroid, or anti-infective/antiseptic agent. (Id. 19:15-46).

PRINCIPLES OF LAW

Lack of Enablement

"That some experimentation is necessary does not constitute a lack of enablement; the amount of experimentation, however, must not be unduly extensive." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1212 (Fed Cir. 1991).

Anticipation

"The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition." *In re Spada,* 911 F.2d 705, 708 (Fed. Cir. 1990)

Obviousness

"Selecting a narrow range from within a somewhat broader range disclosed in a prior art reference is no less obvious than identifying a range

that simply overlaps a disclosed range." *In re Peterson*, 315 F.3d 1325, 1329-1330 (Fed. Cir. 2003).

Moreover, when "the claimed ranges are completely encompassed by the prior art, the conclusion is even more compelling than in cases of mere overlap." *Id at 1330.*

ANALYSIS

I. The Enablement Rejection.

Claims 1-19, 21-23 and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

The Examiner found that "the specification, while being enabling for some agents, does not reasonably provide enablement for the broad phrase of 'an agent.'" (Non-Final Rejection, Nov. 30, 2006, p. 2, incorporated by reference in Final Rejection, May 9, 2007, p. 2). In consideration of the factors set for in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988), the Examiner particularly found that one of ordinary skill in the art would be burdened with undue experimentation to determine all agents in combination with cyclodextrin derivatives being capable of delivery to the eye. (Id. 2-3).

The Appellants assert that the Examiner's enablement rejection was erroneous because "[t]he specification cites about 400 different examples of therapeutically active agents." (App. Br. 4) (citing Specification p. 6, ll. 22 to p. 15, ll. 15). The Appellants also assert that the specification demonstrates that cyclodextrin and its derivatives deliver the active agent prednisolone to the back of the eye. (Id.). The Appellants further assert that "known literature provides ample guidance to a person of ordinary skill to

determine which compounds are likely to work in the claimed methods." (Id. at 5).

We agree that the Appellants' claims are enabled by the specification. As the court in *Martin v. Johnson*, 454 F.2d 746, 751 (1972) (citations omitted) stated:

> To satisfy §112, the specification disclosure must be sufficiently complete to enable one of ordinary skill in the art to make the invention without undue experimentation, although the need for a minimum amount of experimentation is not fatal. . . . Enablement is the criterion, and every detail need not be set forth in the written specification if the skill in the art is such that the disclosure enables one to make the invention.

The specification describes that "the use of cyclodextrins in pharmaceutical compositions is well known in the art." (Specification p. 3, ll. 7-8). The specification also describes that "[t]he use of cyclodextrin and cyclodextrin derivatives in ophthalmic formulations is also known." (Id. p. 3. ll. 20-21). Further, as the Appellants have asserted, the specification provides numerous examples of therapeutically active agents. (Id. pp. 6-7).

The Examiner has not provided sufficient reasoning as to why one skilled in the art of ophthalmic pharmaceuticals would not be able to determine without undue experimentation which ophthalmic agents would work in the claimed method. The Examiner has therefore not satisfied the initial burden of providing reasoning which would substantiate a rejection based on lack of enablement.

Consequently, we reverse the Examiner's rejection of claims 1-19, 21-23 and 26 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

II. The Anticipation Rejections.

Claims 1-15, 19, 21-23 and 26 stand rejected as being anticipated under 35 U.S.C. § 102(b) over Guy. The Examiner found that Guy teaches the use of the claimed cyclodextrin derivatives, e.g., hydroxypropyl cyclodextrin, in combination with a therapeutically active agent, e.g., prednisolone acetate, in an ophthalmic/pharmaceutical formulation for the treatment of ophthalmic disorders. (Non-Final Rejection, June 29, 2006, p. 2, incorporated by reference in Final Rejection, May 9, 2007, p. 2) (citing 1:38-65, 2:55, 3:1-10, 3:30-37, 4:1-15).

The Examiner additionally rejected claims 1-19, 21-23 and 26 as being anticipated under 35 U.S.C. § 102(b) over Lyons. For this rejection, the Examiner similarly found that Lyons teaches the use of the claimed cyclodextrin derivatives in combination with prednisolone acetate and additionally with HPMC (as recited in Appellants' claims 16-18) in an ophthalmic formulation for the delivery to the eye. (Non-Final Rejection, Nov. 30, 2006, p. 4, incorporated by reference in Final Rejection, May 9, 2007, p. 2) (citing Lyons p. 10, ll. 8-13, p. 12, ll. 11-26 and p. 14 Table).

The Appellants do not dispute the Examiner's finding that Guy and Lyons each disclose the components of the composition recited in the Appellants' respective claims. Nor do the Appellants dispute the finding that each reference describes that their compositions are administered topically to the eye. Rather, as to both rejections, the Appellants assert that the claims are not anticipated because "[n]either of the references teaches administration of the composition *for the purpose of delivering the drugs to*

the particular structures of the eye cited in the claims." (App. Br. 7) (emphasis added).

This argument is not persuasive. It is not in dispute that the claimed composition of claim 1 has been applied to the eye for therapeutic purposes in the cited prior art. The claimed method of delivering a composition to structures of the eye in or posterior to the vitreous humor is, at best, a different intended use of a previously known topical ophthalmic composition which inherently functioned in the same way as now claimed. As the Federal Circuit has stated, "The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition." *In re Spada,* 911 F.2d 705, 708 (Fed. Cir. 1990).

Consequently, we find that the Appellants have not established that the Examiner erred in (a) rejecting claims 1-15, 19, 21-23 and 26 as being anticipated by Guy, and (b) rejecting claims 1-19, 21-23 and 26 as being anticipated by Lyons.

III. The Obviousness Rejection.

Claims 16-18 stand rejected as being obvious under 35 U.S.C. § 103(a) over the combination of Guy and Loftsson.

Representative claim 16 reads as follows:

> 16. The method of claim 5 which further comprises hydroxypropylmethylcellulose having a concentration less than 1%.

Claim 5 reads as follows:

> 5. The method of claim 1 wherein said therapeutically active agent is not administered to reduce intraocular pressure.

The Examiner found that Guy differs from the claimed invention because Guy does not describe using HPMC in the ophthalmic composition. (Non-Final Rejection, June 29, 2006, p. 2, incorporated by reference in Final Rejection, May 9, 2007, p. 3). However, the Examiner found that Loftsson teaches the use of the claimed HPMC in combination with the claimed cyclodextrin and a therapeutically active agent, e.g., steroid, in an ophthalmic formulation. (Id.).

According to the Examiner, it would have been obvious to a person of ordinary skill in the art to incorporate HPMC into the teaching of the primary reference because Loftsson describes that addition of HPMC to the claimed cyclodextrin well known in the art. (Id.). The Examiner also found that one skilled in the art would have been motivated to combine the teachings of the references because references represent analogous art of cyclodextrin-containing ophthalmic formulations. (Id. at 4). The Examiner further found that the Appellants did not present evidence to establish the unexpected or unobvious nature of the claimed invention. (Id.).

Here again, the Appellants assert that the Examiner's rejection is erroneous because "[u]sing cylodextrin derivatives to deliver drugs to the back of the eye is not taught or suggested in the prior art." (App. Br. 7). The Appellants additionally assert that the Examiner failed to explain how the prior art composition is used "in such a way that a therapeutically effective amount of the required drug would be delivered to the back of the eye structure." (Id.).

These arguments are unpersuasive. The Examiner found that Guy teaches the use of the claimed cyclodextrin derivatives with a therapeutically active agent, e.g., prednisolone acetate, in a topical ophthalmic pharmaceutical formulation. Additionally, the Examiner found that Loftsson describes adding HPMC to an ophthalmic composition comprising a cyclodextrin and therapeutically active agent. The Examiner further found that the combination of Loftsson's HPMC with Guy's topical ophthalmic composition would have been obvious to one skilled in the art at the time of the invention because the combination of HPMC with cyclodextrin compositions was well known in the art and the references represent analogous art. Additionally, Loftsson describes that adding HPMC to a cyclodextrin-containing ophthalmic compositions enhances the solubilizing and stabilizing effects of cyclodextrin. (Loftsson 1:12-15). The Appellant has not challenged these findings.

Loftsson also describes the polymer (HPMC) comprises 0.001-5%, preferably from about 0.01 to about 0.5% of the composition (Id. 4:21-30). This disclosed range encompasses the concentration described by claim 16, i.e., "less than 1%." As the Federal Circuit has affirmed, "Selecting a narrow range from within a somewhat broader range disclosed in a prior art reference is no less obvious than identifying a range that simply overlaps a disclosed range." *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003). Moreover, when "the claimed ranges are completely encompassed by the prior art, the conclusion is even more compelling than in cases of mere overlap." *Id.*

Therefore, the method of claim 16 recites a topically administered composition that would have been obvious to a skilled artisan at the time of the invention. As the Examiner stated, "the appellant is using the same composition as [the] prior art, therefore it is expected that such composition would inherently act the same as the composition of the instant application." (Ans. 6). The Appellants have put forth no persuasive evidence that this finding is incorrect. *See In re Spada,* 911 F.2d 705, 708 (Fed. Cir. 1990).

Consequently, we do not find that the Appellants have established that the Examiner erred in rejecting claims 16-18 as obvious over the combination of Guy and Loftsson.

Accordingly, we affirm the Examiner's rejections.

CONCLUSION OF LAW

On the record before us, the Appellants have not shown error on the part of the Examiner regarding the anticipation rejections of claims 1-19, 21-23 and 26, and the obviousness rejections of claims 16-18. The prior art anticipated a method of topically administering a known topical ophthalmic composition to structures of the eye in or posterior to the vitreous humor. Additionally, it would have been obvious to one of ordinary skill in the art at the time the invention was made to topically administer a known topical ophthalmic composition to structures of the eye in or posterior to the vitreous humor.

However, regarding the enablement rejection of claims 1-19, 21-23 and 26, the Appellants have established that the Examiner erred in determining that the specification does not provide sufficient guidelines to enable of one of ordinary skill in the art to know, without undue

experimentation, which therapeutically active agents may be administered by the claimed method.

DECISION

The Rejection of claims 1-19, 21-23 and 26 under 35 U.S.C. § 112, first paragraph, as being unpatentable for failing to comply with the enablement requirement is REVERSED.

The Rejection of claims 1-15, 19, 21-23 and 26 under 35 U.S.C. § 102(b) as being unpatentable over Guy is AFFIRMED.

The Rejection of claims 1-19, 21-23 and 26 under 35 U.S.C. § 102(b) as being as being unpatentable over Lyons is AFFIRMED.

The Rejection of claims 16-18 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Guy and Loftsson is AFFIRMED.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv) (2006).

AFFIRMED

TORCZON, *Administrative Patent Judge*, concurring.

I join the majority in affirming the anticipation and obviousness rejections. I would not reach the enablement rejection. *Cf. Leggett & Platt, Inc. v. VUTEk*, 537 F.3d 1349, 1356 (Fed. Cir. 2008) (not reaching § 112 issue after affirming anticipation and obviousness grounds of invalidity).

rvb

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